

Cure CLCN4 Pilot Grant Program 2023. Guidelines

The Cure CLCN4 Pilot Grant Program provides a 1.5 year grant to support research on *CLCN4*-related neurodevelopmental condition (*CLCN4*-NDC). We will award a total of £150,000 (2-3 awards of £50,000-£75,000/each).

About Cure CLCN4

Cure CLCN4 is a UK-registered charity (1190344) that aims to support scientific research to further our understanding of the biology of *CLCN4*-NDC and thus facilitate development of new and effective treatments for affected individuals. Further, we aim to act as a support hub for individuals with a diagnosis of *CLCN4*-NDC and their families and to raise awareness of *CLCN4*-NDC among the scientific and medical community. You can learn more about us by visiting our website at www.cureclcn4.org

Overview

CLCN4-related neurodevelopmental condition (*CLCN4*-NDC) is one of the more recently discovered rare X-linked monogenic disorders. It is caused by inherited or *de novo* pathogenic variants of the *CLCN4* gene. It affects both females and males. Clinical features in affected individuals include intellectual disability, behavioral, and psychiatric abnormalities, epilepsy, movement disorders and gastrointestinal issues. *CLCN4*, one of the nine members of the *CLCN* gene family encoding anion-transporting membrane proteins, encodes the CIC-4 protein, a voltage-dependent 2Cl⁻/H⁺ exchanger localized in intracellular endo-/ lysosomal membranes and is thought to function in ion homeostasis and intracellular trafficking. Although known to have critical functional interactions with CIC-3, encoded by the disease-implicated gene *CLCN3*, the function of CIC-4 is far from being well understood. Improving our understanding of the biological function of CIC-4, and how different *CLCN4* variants affect the functionality of the protein, is an essential step to uncover the pathomechanism(s) and pathophysiology of *CLCN4*-NDC and to develop disease-specific therapeutic approaches.

Thus, Cure CLCN4 is seeking grant applications towards new or existing projects aimed at improving our knowledge of the fundamental biology of *CLCN4*-NDC.

Level and duration of funding

We will be awarding a total of £150,000 (2-3 grants of £50,000-£75,000/each). The award will be for **18 months**, with an option to apply for a no-cost extension of 6 months (details on the extension will be provided following the award decision). The proposed funding period is from **1st April, 2024 to 1st October, 2025**.

While the request for applications is broad in scope, we are especially interested in projects covering the following areas:

1. Understanding of the basic biology and function of the CLCN4 protein.
2. Functional characterization of new *CLCN4* variants and/or variants of unknown significance.
3. Characterization of animal models of *CLCN4*-NDC; with particular interest in the characterization of the Cure CLCN4-funded rat models available from the INFRAFRONTIER repository (for details please email us at rebeca.rf@cureclcn4.org). Non-rodent animal models will also be considered.

The ultimate objective of this grant call is to support projects aimed at helping uncover the pathophysiology of *CLCN4*-NDC, and with it, to pave the way for the development of novel and targeted therapeutic approaches to effectively manage the condition.

Application Instructions and Review Procedure

Eligibility criteria

- All applicants and key collaborators must **hold a Ph.D., M.D. or equivalent** degree and have a faculty position or equivalent at a college, university, medical school, or other research facility.
- There are **no citizenship/country requirements**.
- Proposed projects should be **strictly on CLCN4-related research**. The implications of the research on this field should be clearly stated in the application.

Instructions for submission

- **Downloading the application documents:** you can find and download the application on our website (www.cureclcn4.org/2023_grant_program). Alternatively, you can email us at rebeca.rf@cureclcn4.org for a copy of the application.
- **Format:** use Arial typeface, font size of 10 and black font color. Text should be 1.5 spaced.
- **Submission:** Completed and **signed** applications must be in PDF format and emailed to rebeca.rf@cureclcn4.org no later than **5pm (GMT) on 15th December 2023**. A list of items to be submitted can be found below.

Checklist of items to be submitted

- Main application document (in pdf format)
- Biosketch of the Principal Investigator (PI) and any key personnel. The PI must include accurate and complete information regarding all other sources of grant support (current and pending), including title, abstract, annual, and total amount of grant, inclusive funding period, and percent effort.
- Bibliography (max. 3 pages, submit in pdf format, include ORCID ID)
- Appendix (max. 3 pages, submit in pdf format)

If the proposal includes animal models, proof of your ethics approval and adherence to animals in research regulations (e.g. IACUC letter of approval).

Grant review procedure

Applications that meet the eligibility criteria will be judged by a panel of scientific experts and Cure CLCN4. Grants will be reviewed based on the relevance of the proposal to the goals of the grant call and Cure CLCN4's objectives, the quality and robustness of the scientific content and the qualifications and experience of the applicant. Projects will be assessed according to the following criteria:

- **Relevance:** alignment with the current scientific understanding of *CLCN4*-NDC and potential to provide novel insights/address unmet needs in the field.
- **Rationale:** scientific basis and significance of the project, how the project addresses current gaps in knowledge, and adequate use/referencing of previous studies or evidence supporting your research approach.
- **Impact:** how findings could contribute to advancing our understanding of the biology of *CLCN4*-related condition, moving the field forward, improving diagnostic methods, developing novel therapies, or enhancing patient care.
- **Feasibility:** assessment of the feasibility of the proposed research project, taking into account personnel, technical, and economic factors, and ways of addressing any potential challenges or constraints.

Notification and grant payment

Successful applicants will be contacted **via email by 29th February 2024**. Funds will be issued through a cost reimbursement mechanism (i.e. based on actual costs incurred). Details of invoicing schedules and reporting requirements will be made available upon award.

Allowable costs

If required, institutions can take up to 10% of overhead/indirect costs from the award totals (with the exception of UK-based awardees*). Awarded amounts will not exceed £75,000.

Allowable direct costs

Salary for PI (**early-career researchers only)
Salary/stipend for graduate student/postdoc/technician
Travel to the Cure CLCN4 conference
(up to £1,000)
Laboratory supplies & other research expenses
10% in overhead costs (except UK awardees)
Payment of open access publication fee

Unallowable costs

Consultant costs
Tuition
General office supplies, institutional
administrative charges
Pre-award charges
Equipment > £4,000
Professional membership dues
Any other expense not directly related to
the project

*Indirect costs of charity-funded research in UK universities are covered by the Charity Research Support Fund (in England). Similar funding is provided in Scotland, Wales, and Northern Ireland.

**We define early-career researchers as someone who is i) within eight years of their PhD award, or equivalent professional training; or ii) within six years of their first academic appointment (the first full or part time paid employment contract that lists research or teaching as the primary function).

Reporting and evaluation

For the purposes of monitoring progress and performance, and upon acceptance of the grant, successful applicants agree to our post-award requirements:

- Submission of **two post-award written reports**, at 9 and 18 months after receipt of the grant. A reminder of the submission dates and templates for the report will be emailed to awardees.
- Grant recipients are required to **meet with Cure CLCN4 (via videocall)** at 6, 12 and 18 months after receipt of the award (and at 24 months in case of a 6-month no-cost extension).
- All awardees are also required to meet to discuss their progress, share findings, and exchange ideas with fellow awardees. These meetings will be conducted in the presence of a representative from the awarding body, Cure CLCN4, to ensure accountability and to facilitate effective communication. Meetings will take place at 6, 12 and 18 months after receipt of the award.
- Presentation of the grant-funded project at the annual **Cure CLCN4 Scientific Meeting**.
- You agree to appear on the Cure CLCN4 website news section and on social media as part of a feature on successful grant awardees.

Publication

- All original, peer-reviewed research articles that are supported in whole, or in part, by Cure CLCN4 should be **published with open access** to ensure that findings can be freely accessed, used, and built on (*the funds of this grant can be used to cover the open access fee).
- Research publications must **acknowledge funding** received from Cure CLCN4.

Our commitment to Diversity, Equity, and Inclusion

Cure CLCN4 provides equal opportunities to all applicants for funding without regard to race, religion, color, age, sex, pregnancy, national origin, sexual orientation, gender identity, genetic disposition, neurodiversity, or disability.

For questions regarding the application please contact:

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